

### **REMARKS**

Reconsideration of this application, as amended, is respectfully requested. The Applicants wish to draw the Examiner's attention to the applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof.

The Applicants note that the Examiner did not return an executed PTO 1449 form for the 6<sup>th</sup> Supp. IDS that was hand-delivered to the Examiner on September 9, 2002. The Applicants request that the Examiner fully execute the PTO 1449 form for the 6<sup>th</sup> Supp. IDS and return a copy of the executed PTO 1449 form to the undersigned representative. Copies of the 6<sup>th</sup> Supplemental IDS, and associated PTO 1449 form are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

The specification has been amended to update the priority claim. No new matter has been added to the application as a result of this amendment.

Claims 150 and 170 were pending in this application. These claims were cancelled and new claims 433-470 were added to further clarify the Applicants' invention. The new claims are fully supported in the previously pending claims, and thus do not constitute new matter. The new claims are supported, for example, by original claims 189-265, 431 and 432 and the specification on page 20, line 23 to page 22, line 22; page 58, line 22 to page 61, line 18; page 69, line 26 to page 70, line 8; page 76, line 18, to page 80, line 27; and Figure 24. Thus, the new claims do not constitute new matter.

Turning to the office action, claims 155 and 170 were rejected under 35 U.S.C. section 112, second paragraph, for indefiniteness. Claims 155 and 170 also stand rejected under 35 U.S.C. section 103(a) as being obvious based on Yguerabide (U.S. Patent No. 6,214,560)("Yguerabide") in view of Hainfeld (U.S. Patent No. 5,521,289)("Hainfeld"). The aforementioned claims have been cancelled and thus the rejections are moot. The Applicants respectfully submit that the cited references cannot be applied to support a rejection of the new claims.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light

scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. The Examiner also alleged that Hainfeld described small organometallic probes. The discussion is found starting in col. 3, line 23, of Hainfeld. There is no disclosure or suggestion in either Yguerabide or Hainfeld of any satellite probe and kit containing the same as recited in the present claims.

Furthermore, there is no discussion or suggestion of the Applicant's ageing process "wherein the oligonucleotides are attached to the nanoparticles in an ageing processing comprising contacting the oligonucleotides with the nanoparticle in an aqueous solution for a period of time sufficient to allow some of the oligonucleotides to bind to the nanoparticle; and contacting the oligonucleotides and nanoparticle in an aqueous salt solution for an additional period of time sufficient to enable additional oligonucleotides to bind to the nanoparticle." See, for instance, new claim 461. Nanoparticle-oligonucleotide conjugates prepared by this ageing process surprisingly exhibit melting (dehybridization) profiles that are extremely narrow compared to the profiles obtained using the same oligonucleotides not attached to nanoparticles, and extraordinary selectivity (detection as little as a single base difference) and sensitivity (detecting as little as 10 femtomoles of nucleic acid without amplification) have been obtained using these conjugates in such assays (see particularly Examples 5, 7 and 19) of the application. These conjugates are surprisingly more stable compared to conjugates made without the aging step (see, e.g., Example 3 of the application).

For at least the above reasons, the Applicants submit that neither Yguerabide nor Hainfeld, alone or in combination, can be applied to support any rejection of the new claims.

Reconsideration of this application and a favorable determination is respectfully requested. The Examiner is invited to contact the undersigned if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Respectfully submitted,

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**APPENDIX A**

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>00-653-A</b>	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	ALLOWED
<b>00-713-B1</b>	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	ALLOWED
<b>00-713-C</b>	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
<b>00-713-I</b>	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
<b>00-713-I-1</b>	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	
<b>00-713-I-2</b>	09/957,318 9/20/01	See 00-713-I-1	ALLOWED
<b>00-713-I-3</b>	09/957,313 9/20/01	See 00-713-I-1	U.S. Patent No. 6,645,721, issued 11/11/03
<b>00-713-I-4</b>	09/966,491 9/28/01	See 00-713-I-1	U.S. Patent No. 6,610,491, issued August 26, 2003
<b>00-713-I-5</b>	09/966,312 9/28/01	See 00-713-I-1	U.S. Patent No. 6,673,548, issued January 6, 2004
<b>00-713-I-6</b>	09/967,409 9/28/01	See 00-713-I-1	U.S. Patent No. 6,740,491, issued May 24, 2004
<b>00-713-I-7</b>	09/974,500 10/10/01	See 00-713-I-1	U.S. Patent No. 6,709,825, issued March 23, 2004
<b>00-713-I-8</b>	09/974,007 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-9</b>	09/973,638 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-10</b>	09/973,788 10/10/01	See 00-713-I-1	U.S. Patent No. 6,720,411, issued April 13, 2004
<b>00-713-I-11</b>	09/975,062 10/11/01	See 00-713-I-1	U.S. Patent No. 6,677,122, issued January 13, 2004
<b>00-713-I-12</b>	09/975,376 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-13</b>	09/975,384 10/11/01	See 00-713-I-1	PENDING

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<b>00-713-I-14</b>	09/975,498 10/11/01	See 00-713-I-1	ALLOWED
<b>00-713-I-15</b>	09/975,059 11/11/01	See 00-713-I-1	ALLOWED
<b>00-713-I-16</b>	09/976,601 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-17</b>	09/976,968 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I-18</b>	09/976,971 10/12/01	See 00-713-I-1	U.S. Patent No. 6,682,895, issued 1/27/04
<b>00-713-I-19</b>	09/976,863 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-20</b>	09/976,577 10/12/01	See 00-713-I-1	U.S. Patent No. 6,720,147, issued April 13, 2004
<b>00-713-I-21</b>	09/976,618 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I-22</b>	09/981,344 10/15/01	See 00-713-I-1	ALLOWED
<b>00-713-I-23</b>	09/976,900 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-24</b>	09/976,617 10/12/01	See 00-713-I-1	U.S. Patent No. 6,730,269, filed May 4, 2004
<b>00-713-I-25</b>	09/976,378 10/12/01	See 00-713-I-1	PENDING
<b>00-713-i-26</b>	10/410,324 04/10/03	See 00-713-I-1	PENDING
<b>00-713-L</b>	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES	U.S. Patent No. 6,495,324, issued 12/17/02

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		HAVING OLIGONUCLEOTIDES ATTACHED THERE TO AND USES THEREFORE	
00-713-M	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERE TO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
00-714-G	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
00-715-A	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTIDES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	ALLOWED
00-1085-A	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
00-1085-G	U.S.S.N. 10/640,618 Filed 8/13/03	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	
00-1086-A	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF	U.S. Patent No. 6,602,669,

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		DETECTION BY ENHANCEMENT OF SILVER STAINING	Filed 8/5/03
<b>00-1272-C</b>	U.S.S.N. 10/008,978 Filed 12/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garimella, Li, Park, Lu/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREOF	PENDING
<b>01-565-A</b>	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguyen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS AND CO- POLYMERS	PENDING
<b>01-599-A</b>	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES	PENDING
<b>01-661-A</b>	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
<b>01-661-C</b>	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
<b>01-661-E</b>	U.S.S.N. 10/397,579 3/26/03	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING



<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>01-1565-A</b>	U.S.S.N. 10/266,983 Filed 10/08/02	Park, Taton, Mirkin/ARRAY- BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	PENDING
<b>01-1633-A</b>	U.S.S.N. 10/266,983 Filed 10/8/02	Park, Taton, Mirkin/NANOPARI CLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFOR	PENDING
<b>01-1705-A</b>	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO- BARCODES BASED ON OLIGONUCLEOTI DE-MODIFIED NANOPARTICLES	PENDING
<b>02-338-B</b>	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTICHA NNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING
<b>02-338-C</b>	10/431,341 5/7/03	Cao, Jin, Nam, Mirkin/MULTICHA NNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING